

### **REMARKS/ARGUMENTS**

Claims 1-3 and 5-7 have been amended solely in an effort to advance prosecution. Claims 8-16 have been newly added in an effort to more explicitly claim certain embodiments of the present invention. Support for the new claims may be found, for example, on pages 4, 7, 8 of PCT Pub. No. WO 2004/047813 corresponding to PCT App. No. PCT/IL2003/000159.

Applicants acknowledge the withdrawal of all previous rejections. Applicants understand that claims 1-3 and 5-7 were most recently rejected as obvious under 35 U.S.C. § 103 over U.S. Pat. App. Pub. No. 2002/0136755 to Tyrrell et al. (Tyrrell) in light of U.S. Pat. No. 4,742,046 to Bliah (Bliah), U.S. Pat. No. 5,543,154 to Rork et al. (Rork), and U.S. Pat. No. 5,780,046 to Humber et al. (Humber). For at least the reasons set forth in this Amendment, Applicants respectfully disagree with the Patent Office's position that these references would have enabled a person having ordinary skill in the art at the time of the invention to derive the as-claimed subject matter as defined by claim 1 and its dependents and new claim 11 and its dependents.

The Patent Office's current rejection appears to be based on the following three main points:

- 1) The claims currently on file cover any adhesive, topically administrable composition.
- 2) The references cited teach that the herbs may be used in topical compositions applied onto the skin.
- 3) The references teach that the herbs are "medical adhesives."

The second and third points – which require an examination of the cited references – are discussed below. With respect to the first point, however, Applicants have amended the only independent claim to explicitly and affirmatively recite a structural limitation regarding the property of the claimed composition – i.e., that the “muco-adhesive solid therapeutic composition adheres to mucosal tissue.” This structural limitation further defines the claimed invention and cannot be ignored. *See, e.g., Union Oil Co. of Cal. v. Atl. Richfield Co.*, 208 F.3d 989, 995-96 (Fed. Cir. 2000) (holding that composition claims directed to a composition “suitable for combustion in an automotive engine” were **not** anticipated by prior art compositions related to other types of fuels, like aviation and racing fuels). Support for this amendment may be found throughout the specification, e.g., PCT Pub. No. WO 2004/047813 at 1-3 & 8-9.

Furthermore, new claim 11 (and its dependents) relate to a method of treating a mucosal tissue in a patient that includes contacting a mucosal lesion with a therapeutically effective amount of a muco-adhesive solid therapeutic composition. This limitation is not taught, suggested, or hinted at in the cited references.

The references do not render the particularly claimed limitations to be obvious, and they are discussed in the order listed in the Office Action: Tyrrell, Bliah, Rork, then Humber.

The Office Action noted that Tyrrell “teaches a composition for skin contact comprising about 0.1 to about 40% by weight of viscosity enhancers of PVP/decane copolymer, PVP/eicosene, PVP/hexadecane copolymer (paragraph 0023), about 0.1 to

about 10% by weight of one or more extracted botanical actives of *Echinacea purpurea*, *Centella asiatica* (paragraph 0025).” (Office Action at 3.) The Office Action further alleged: “Compositions maintain their integrity and stability in a solid state for transfer to skin, including adhesion of the composition to the skin (paragraph 0037).” (*Id.*) As acknowledged by the Office Action, Tyrrell does not teach the other ingredients.

Applicants highlight the following points regarding Tyrrell. Tyrrell focuses on absorbent articles, in particular diapers, to which extracted botanical actives, such as *Echinacea purpurea*, *Centella asiatica* and a long list of other herbs, are added. Tyrrell’s Abstract, for example, states: “The present invention relates to **absorbent articles** including non-aqueous compositions for protecting the barrier function of the skin.” And Tyrrell provides the extensive laundry list of “suitable” extracted botanical actives: “Examples of suitable extracted botanical actives are actives extracted from echinacea, yucca glauca, willow herb, basil leaves, Turkish oregano, carrot root, grapefruit fruit, fennel fruit, rosemary, thyme, blueberry, bell pepper, black tea, blackberry, black currant fruit, Chinese tea, coffee seed, dandelion root, date palm fruit, ginkgo leaf, green tea polyphenols (i.e. including epicatechin gallate and epigallocatechin 3-O-gallate), hawthorn berries, licorice, oolong tea, sage, strawberry, sweet pea, tomato, vanilla fruit, neohesperidin, quercetin, rutin, morin, myricetin, chlorogenic acid, glutathione, glycyrrhizin, absinthe, arnica, centella asiatica, chamomelle, comfrey, cornflower, horse chestnut, ivy (*Herdera helix*), magnolia, mimosa, oat extract, pansey, scullcap, seabuckthorn, white nettle, witch hazel and any combinations thereof.” (Tyrrell at

¶ [0025].) In fact, it appears that the only disclosure of *Centella asiatica* – a component of the pending claims – cursorily appears in the boilerplate list reproduced in paragraphs [0025] and [0116]. Similarly, the only disclosure of *Echinacea purpurea* – a component of the pending claims – cursorily appears in the same boilerplate list reproduced in those paragraphs. That is, Tyrrell provides **no** working examples containing either of these herbs, even individually and not in combination.

But even assuming (solely for the sake of argument) that Tyrrell did provide some enabling guidance (other than the mere mention of these herbs), there is nothing in Tyrrell that would teach or suggest adhesion of a composition as claimed to any type of mucosal tissue. Although Tyrrell does mention (e.g., para. [0037]) that the composition **may** adhere to **skin**, it should be recognized that mucosal tissues is generally a much more difficult substrate for adhesion, e.g., due to the extremely humid as well as possibly enzymatically-active environment. Therefore, the requirements of a muco-adhesive composition as claimed are completely different compared to a skin-adhesive composition as disclosed. Furthermore, there is an inherent inconsistency in finding that Tyrrell teaches and encourages adhesion of any type (regardless of substrate) while the purpose of Tyrrell's invention is to prevent and alleviate skin irritations associated with the use of the absorbent articles (like diapers). One would expect that an enhanced adhesion to the skin may itself promote skin irritation. For example, Tyrrell teaches that not all types of adhesion are appropriate, specifically noting that fracturing or flaking is preferred to "rubbing off onto the skin" from the absorbent article.

Furthermore, there is nothing in Tyrrell that even hints at the additional limitations present in claim 1's dependent claims, including new claims 8-10. And Tyrrell similarly does not teach, suggest, or hint at the limitations of new claims 11-16.

According to the Office Action, Bliah "teaches lectins obtained from *Sambucus nigra* (column 1, line 15), in form of a pharmaceutical composition to said animals or man in pharmaceutically acceptable carriers (in column 4, lines 15-16 and 19-20), for topical application, which are formulated in a semisolid material such as oleaginous ointment bases (column 7, lines 43-45).

Applicants highlight the following points regarding Bliah, which the Patent Office has not alleged to contain any element of the pending claims except the bare disclosure of *Sambucus nigra* itself. As an initial matter, it is the lectins obtained from the *Sambucus* (and not the *Sambucus* itself) that is key to the anti-viral compositions of Bliah's disclosure: "The present invention relates to methods and compositions for inhibiting the infectious activity of viruses by the use of lectins. More specifically, it relates to the use of lectins obtained from *Sambucus nigra* for inhibiting the activity of enveloped viruses." (Bliah at 1:12-16.) Furthermore, Bliah fails to teach, suggest, or hint at any adhesive properties of a composition – not of *Sambucus nigra* alone, and certainly not of a composition containing, among other things, a mixture of *Sambucus nigra*, *Centella asiatica* and *Echinacea purpurea*. And while Bliah may disclose a topical application of a composition containing a lectin derived from *Sambucus nigra* for treatment or prevention of viral-based diseases (e.g., *id.* at 4:10-21), the reference is completely silent

with respect to any adhesive properties – particularly adhesive properties on mucosal tissue as presently claimed in the currently pending claims. Lastly, it is unclear why a person of ordinary skill in the art would even consider – under any rationale – combining selected elements from an absorbent article (like the diapers disclosed in Tyrrell) with an anti-viral composition (like disclosed in Bliah).

According to the Office Action, Rork teaches “an acrylic acid called CARBOPOL 974P (column 4, lines 34- 37), excipients such as lactose, polyvinylpyrrolidone to make tablets, active agents from about 0.01% to about 75% of the core weight (column 7, lines 26, 28-29, 32, 36-37), polymeric coating is applied to and adheres to the entire surface of the core (column 9, lines 8-9), povidone (K29-32) (column 10 line 59), tablets were rolled to prevent sticking (in column 11, lines 5-6).” (Office Action at 3-4.)

While Rork may disclose certain excipients for use in a time-release drug delivery composition, it in no way mentions, hints, or suggests the as-claimed invention, including, among other things, a failure to mention any of the herbal extracts named in the pending claims. Furthermore, there is no disclosure of any adhesive properties of the composition, and especially not with respect to mucosal tissue as presently claimed. Indeed, Rork explains that the polymeric coating is merely to used to “adhere[] to the entire surface of the core” and that “[a]pertures are produced in the coating to expose the core, using either a drill, a coring device or any other pharmaceutically accepted means.” (Rork at 9:8-11.) There is nothing, therefore, that would indicate, hint, or suggest that the disclosed polymer composition (or any of its ingredients) would adhere to muscosal

tissue, let alone indicate, hint, or suggest that an as-claimed composition would be beneficial or desirable in any way. And much like the other cited references, Rork is completely silent with respect to any adhesive properties on mucosal tissue as presently recited in the currently pending claims.

According to the Office Action, Humber “teaches formulation for tablet with hydroxypropyl cellulose (column 9, line 1).” (Office Action at 4.) While it is true that Humber –in a single example – mentions the use of hydroxypropyl cellulose, it is unclear how that disclosure relates to any of the cited references. There is no articulated rationale to combine this reference with the others. For example, Humber is also completely silent with respect to any adhesive properties on mucosal tissue as presently claimed in the independent and new dependent claims.

It is apparent that the cited references fail to teach or enable with any reasonable direction or guidance: (1) A combination as claimed, including, among other things, the three specified herbs; (2) Any adhesive properties of the as-claimed combination; (3) Any suitability for application in mucous membranes, as claimed; and (4) Any reasonable rationale to combine together selected portions of the diaper of Tyrrell, the ointment of Bliah and the tablets of Rork and Humber.

Although it has not been expressly mentioned before, it should be understood that because no adhesive properties are taught by the references, the specifically claimed adhesive tablet of claim 2 is similarly not taught or enabled by the combination of cited references. That is, that structure does not appear to be present in any of the cited art.

Furthermore, the Office Action seems to argue that claim 3 is obvious because a person of ordinary skill in the art would reasonably expect that the topical ingredients of *Sambucus nigra*, *Centella asiatica* and *Echinacea purpurea* could be not only combined but optimized, as routine practice, in the claimed amounts of each specific ingredient in the composition. Because the technical disclosures and applications of the cited references are so disparate, it cannot fairly be determined that the selected combination could be derived in the as-claimed amounts by mere routine optimization.

Furthermore, we note that the Office Action appears to be requesting evidence of any unexpected results or synergy resulting from the specific amounts of the claimed combination. We believe that the Patent Office has misapplied the *Aller* case. That case stands for the unremarkable proposition that merely changing a temperature or concentration set forth in a single prior art reference is unpatentable. That logic does not apply here, where the Patent Office has already pieced together the inventive combination amongst four separate references. That is, the general conditions of the claimed subject matter are not disclosed in the prior art in a manner comparable to the prior art cited in *Aller*. Any “optimization of general conditions” is too attenuated and far afield from the cited prior art. Regardless, Applicants point out the evidence of nonobviousness in the examples set forth in the specification to show the unexpected results of the claimed combination. *See, e.g.*, Comparative Example 2 and Example 3, PCT Pub. No. WO 2004/047813 at 12-13.



Furthermore, Applicants note that because the newly added method claims are commensurate in scope with the amended composition claims (in that they recite the application of the muco-adhesive composition to mucosal tissue lesions), claims 11-16 are similarly patentable over the cited combination of references. This is especially true with respect to the newly added dependent claims, which recite further limitations that are not taught, suggested, or otherwise found in the prior art references.

If there are any small issues that may be resolved quickly (e.g., using an Examiner's Amendment), the Examiner is encouraged to contact the undersigned.

The Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, in the fee(s) filed, or asserted to be filed, or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Account No. 14-1140, under order no 4110-42.

Respectfully submitted,

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